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(11) CA 2 335 713 (13) A1

(40) 11.01.2001
(43) 11.01.2001

(12)

(21) 2 335 713

(22) 13.04.2000

(51) Int. Cl.[7]: A23L 1/30, A61P 1/00, A61K 31/202, A61K 31/232, A61K 9/48

(85) 15.12.2000

(86) PCT/EP00/03350

(87) WO01/01797

(30) 199 30 030.5 DE 30.06.1999

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(54) FORME POSOLOGIQUE PAR VOIE ORALE
(54) ORAL DOSAGE FORM

(57)

The invention relates to an oral form of administration for foodstuffs as well as for foodstuff supplements and dietary products which comprises several unsaturated fatty acids in a xylose-hardened gelatine capsule with a delayed capsule opening time.

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(12) (19) (CA) **Demande-Application**

(21) (A1) **2,335,713**

(86) 2000/04/13
(87) 2001/01/11

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(51) Int.Cl.[7] A23L 1/30, A61K 9/48, A61K 31/232, A61K 31/202, A61P 1/00
(30) 1999/06/30 (199 30 030.5) DE

(54) **FORME GALENIQUE ORALE**
(54) **ORAL FORM OF ADMINISTRATION**

(57) L'invention concerne une forme galénique orale pour produits alimentaires et compléments alimentaires, ainsi que pour des produits alimentaires, qui comprend des acides gras insaturés plusieurs fois dans une capsule de gélatine durcie par xylose, à temps d'ouverture retardé.

(57) The invention relates to an oral form of administration for foodstuffs as well as for foodstuff supplements and dietary products which comprises several unsaturated fatty acids in a xylose-hardened gelatine capsule with a delayed capsule opening time.

Abstract

Oral Dosage Form

Oral dosage form for food and food supplement as well as dietetics comprising polyunsaturated acids in a xylose-hardened gelatine capsule with a retarded release time.

Oral Dosage Form

The present invention relates to an oral dosage form for food, food supplement, and dietetics.

In the field of food supplement, dietetics and drugs the use of omega-3 polyunsaturated acids is known. Fish oil, linseed oil, cod-liver oil or the like is used to provide said polyunsaturated acids. It is known to supply said substances in gelatine capsules to control the unpleasant taste and to avoid flatulences. To reduce the risk of rapid oxidation and thereby the risk of enlarged toxicity, the oil is mixed with anti-oxidants. Rapid oxidation (becoming rancid) causes not only the development of unhealthy radicals but also reduces the durability of the products. A further problem is the risk that polyunsaturated acids are subject to undesired changes in the stomach and in the duodenum before they enter the small intestine, whereby said acids are not or only partly available in the location of resorption.

WO90/04391 discloses an oral dosage form of omega-3 polyunsaturated acids to overcome the problems of vascular diseases. It is known to supply said acids in soft gelatine capsule shells. WO96/36329 discloses to provide gelatine capsules with a coat of poly ethyl acrylate-methyl-methacrylate. The coat prevents releasing of acid from the capsule already in the stomach.

A pure gelatine capsule prevents neither the risk of changes in the structure of the polyunsaturated acids nor undesired flatulences together with its unpleasant smell.

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EP 2 240 581 B1 discloses a gelatine capsule for pharmaceutical use with a controlled release of active ingredients and a process for the preparation of said gelatine capsules. During said process xylose is added to the liquid gelatine from which afterwards gelatine capsules are formed. Gelatine capsules manufactured according to the process provide retarded release of active ingredients.

The underlying problem of the invention is to provide an oral dosage form for polyunsaturated acids comprising food, food supplement, and dietetics which provides a longer durability for the polyunsaturated acids. Furthermore, the oral dosage form should be admissible under food regulations.

The problem is solved with the features of claim 1.

According to the present invention, polyunsaturated acids are provided in gelatine capsules. The gelatine capsule is hardened with the help of xylose. The hardening provides a retarded opening time of the capsule from about 45 minutes and more.

Typically fatty acids are mixed with antioxidants such as tocopherole, ascorbylpalmitate, propyl gallate and the like. The addition of antioxidants is avoided according to the invention because the xylose hardening prevents fat from "going bad". The peroxidation of the unsaturated acids is an important reaction for going bad of fat. Surprisingly, the dosage form according to the invention provides a low peroxidation, and a considerable delay in time for the fat to become rancid.

The oral dosage form according to the invention provides an undisturbed release of polyunsaturated acids in the intestine after passing the stomach. An unpleasant smell and flatulences are prevented.

Xylose is a well-known adjuvant in food industry which is inter alia re-claimable waste of the cellulose production. Xylose is also suitable as sweetening agent. Furthermore, xylose has a laxative effect.

Omega-3 polyunsaturated acids with a high content of alpha linolenic acid, preferred perilla oil, can be used as polyunsaturated fatty acids. Also the use of fish oil, linseed oil, and gamma-linolenic acid is preferred.

The dosage form according to the invention is very well suited for essential fatty acids of all kinds which are delicate to formation of toxic radicals. For the use of the dosage form the following requirements hold:

- peroxide value < 2,
- no advanced decomposition in the stomach or in the duodenum,
- resorption in the small intestine.

Surprisingly all these requirements are achieved with the dosage form according to the invention.

According to a preferred embodiment of the invention the gelatine capsule is filled with perilla oil. Perilla oil is gained from the oil-containing fruits of the Asian plant perilla fructuence. The perilla oil contains more than 70% of unsaturated fatty acids, in particular α-linolenic acid.

A plurality of scientific studies has proven positive effects for the metabolism of fat (metabolic syndrome) and an antiphlogistic effect in the intestine (Morbus Crohn). Perilla oil has furthermore the advantage of being almost without taste and smell.

Two galenic forms, a pure gelatine capsule and a xylose-hardened capsule, each containing perilla oil, have been tested for their peroxide value at 20°C and 45% humidity for a time period of 12 months. The peroxide value of the xylose-hardened capsule was significantly lower than that of the pure gelatine capsule and did not increase during the testing period but even decreased.

In the study 24 persons took 3 to 6 capsules à 500 mg perilla oil over 4 weeks, no nausea, no stomach pressure, or other symptoms were observed. The persons' ability to taste was not reduced.

Example:

500 mg perilla oil capsule without xylose hardening during the long term test:

	0 Months	3 Months	6 Months	12 Months
Perilla Oil / Perilla Oil mg	498.2	506.2	513.5	486.1
Perilla Oil / α-Linolenic Acid mg	260	264.2	268	253.7
Peroxide Value	2.3	2.5	3.1	3

500 mg perilla oil capsule with xylose hardening during the long term test:

	0 Months	3 Months	6 Months	12 Months
Perilla Oil / Perilla Oil mg	498.7	508.1	513.8	489.2
Perilla Oil / α-Linolenic Acid mg	260.3	265.2	268.2	255.5
Peroxide Value	2.1	2.1	1.6	1

Blister packaging was used during the long term test.

Xylose hardening can be achieved according to EP 0 240 581 B1, especially according to Example 3 of the specification. In an alternative approach it is possible to uniformly spray the capsule with a solution comprising xylose, ethanol and water for a predetermined time interval. During this time the capsules are heated. After spraying a predetermined amount of hardening solution, the capsules are heat-treated for a predetermined time interval. The heat treatment causes the aldehyd function of the xylose to react with the gelatine and to provide a cross-linking. The cross-linking causes the hardening of the gelatine capsule. The finished product provides a structure which inhibits the peroxidation of fatty acids so that the addition of antioxidants is unnecessary.

Amended Claims:

1. An oral dosage form for food, food supplements and dietetics comprising perilla oil in a xylose-hardened gelatine capsule with a retarded release time.

2. The dosage from as recited in claim 1 comprising omega-3 polyunsaturated fatty acids with a high content of alpha linolenic acid.

3. The dosage form as recited in claim 1 or 2, wherein said retarded release time is more than 45 minutes.

4. The dosage form according to one of the claims 1 to 3, wherein said dosage form is operative against diseases of metabolism of fat and/or against intestinal inflammations, such as Morbus Crohn and/or colitis ulcerosa.

5. The dosage form according to one of the preceding claims, wherein the gelatine capsule comprises an ingredient selected from the group consisting of fish oil, linseed oil and gamma linolenic acid.

6. Use of a xylose-hardened gelatine capsule in order to prevent peroxidation of a polyunsaturated fatty acid contained in said gelatine capsule, wherein said gelatine capsule has a retarded release time and is used as oral dosage form for food, food supplements and dietetics.

7. The use as recited in claim 6, wherein said gelatine capsule comprises polyunsaturated fatty acids with a high content of alpha linolenic acid.

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8. The use as recited in claim 7, wherein said gelatine capsule comprises perilla oil.

9. The use according to one of the claims 6 to 8, wherein said retarded release time is more than 45 min.

10. The use according to one of the claims 6 to 9, wherein said gelatine capsule comprises fish oil, linseed oil and gamma linolenic acid.